Glucose Metabolism Drives Histone Acetylation Landscape Transitions that Dictate Muscle Stem Cell Function.

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Public Summary:
The authors find a link between the metabolism of a stem cell and its fate and function. Specifically, how mitochondria use glucose determines remodeling of the histone acetylation landscape of muscle stem cells during tissue regeneration. An enzyme called Pyruvate dehydrogenase (PDH) controls this process and determines the differentiation potential of myogenic progenitors.

Scientific Abstract:
The impact of glucose metabolism on muscle regeneration remains unresolved. We identify glucose metabolism as a crucial driver of histone acetylation and myogenic cell fate. We use single-cell mass cytometry (CyTOF) and flow cytometry to characterize the histone acetylation and metabolic states of quiescent, activated, and differentiating muscle stem cells (MuSCs). We find glucose is dispensable for mitochondrial respiration in proliferating MuSCs, so that glucose becomes available for maintaining high histone acetylation via acetyl-CoA. Conversely, quiescent and differentiating MuSCs increase glucose utilization for respiration and have consequently reduced acetylation. Pyruvate dehydrogenase (PDH) activity serves as a rheostat for histone acetylation and must be controlled for muscle regeneration. Increased PDH activity in proliferation increases histone acetylation and chromatin accessibility at genes that must be silenced for differentiation to proceed, and thus promotes self-renewal. These results highlight metabolism as a determinant of MuSC histone acetylation, fate, and function during muscle regeneration.